Tuberculosis Transmission in Botswana

Lockman and colleagues recently described a study on conventional and molecular epidemiology of tuberculosis in Botswana (4) and found a rate of clustering cases of pulmonary tuberculosis equal to 42%. The authors were surprised by the result, since they expected a higher rate of clustering in a country such as Botswana, where the incidence of tuberculosis is extremely high (over 500 per 100,000). They discussed factors that might have biased the estimation of the extent of recent transmission of tuberculosis and indicated that high population mobility and a rather incomplete epidemiological evaluation of the subjects enrolled likely accounted for the level of transmission recorded.

In our opinion, a crucial issue was not taken into consideration to explain the unexpected rate. In their paper (Materials and Methods), the authors stated that only patients who had both acid-fast bacillus (AFB)-positive and culture-positive sputum were recruited and epidemiologically evaluated. This was probably due to obvious organizational and logistic problems in such a setting, but sputum smears are known to be AFB-positive only in 50 to 70% of culture-positive pulmonary tuberculosis (2). This rate may be affected by specific clinical and epidemiological conditions. HIV-infected tuberculosis subjects, for example, especially those who are seriously immunosuppressed and develope cavitory lesions less frequently (3), are prone to show a lesser degree of AFB-positive sputum smears. These considerations and the high incidence of human immunodeficiency virus-tuberculosis coinfection reported in the study area (65% of the eligible patients) suggest that a sizeable proportion of pulmonary tuberculosis was not included in the epidemiological analysis of Lockman et al.

This may have led to their underestimating the clustering rate in two different ways. First, a relevant portion of pulmonary tuberculosis due to recent transmission might have not been evaluated in the clustering analysis, because the secondary pulmonary cases generated in a cluster would not necessarily have yielded an AFB-positive sputum smear. Second, the infectiousness of smear-negative but culture-positive tuberculosis was recently revalued by Behr et al. (1), who showed that such cases were responsible for about 17% of tuberculosis transmission in San Francisco, Calif., yet the potential sources of transmission with smear-negative but culture-positive pulmonary tuberculosis were not identified by Lockman and co-workers.

In conclusion, we think that fingerprinting limited to tuberculosis cases where the sputum smear was AFB positive should be considered the main confounding factor of the clustering analysis of this study.

REFERENCES

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Authors’ Reply

We thank Bonora et al. for their letter regarding our article, “Molecular and Conventional Epidemiology of Mycobacterium tuberculosis in Botswana: a Population-Based Prospective Study of 301 Pulmonary Tuberculosis Patients” (2).

The authors of the letter suggest a potential source of bias that may have led to underestimation of the true rate of M. tuberculosis restriction fragment length polymorphism (RFLP) clustering in our study population: that only patients with both acid fast bacillus (AFB)-positive and culture-positive tuberculosis (TB) were enrolled, and that a sizeable proportion of persons with culture-positive, AFB smear-negative TB may have been omitted from the study. We agree that it is important to consider how this aspect of our study design may have biased our results.

Indeed, our study was conducted in a country in which initial TB diagnosis depends on sputum microscopy and in which M. tuberculosis culture is not routinely performed. Although inclusion of patients with AFB smear-negative, culture-positive TB in our study would have been optimal, it was not feasible in this setting.

Despite this limitation, however, we believe that the exclusion of persons with smear-negative, culture-positive TB had limited impact on our estimation of clustering. In this and other studies conducted in Botswana, sputum is centrifuged prior to performing smears, which results in an AFB smear-positive yield higher than that observed in many developing-country settings where only direct smears are used. Although human immunodeficiency virus prevalence is high in Botswana, a separate study that was conducted in Botswana during the same time period as this study and that utilized the same TB laboratory found that only 23 (22%) of 103 persons with M. tuberculosis culture-positive TB had negative AFB smears. In that study, 86% of the patients were HIV-positive, and AFB smear status did not differ by HIV status (S. Lockman, N. Hone, T. A. Kenyon, M. Mwasekaga, M. Villathapillia, E. Zell, A. Kirby, W. L. Thacker, D. Talkington, I. N. S. Moura, N. J. Binkin, T. Creek, J. W. Tapper, and the Botswana Respiratory Diseases Working Group, unpublished data). In models of clustering that examine the effects of increasing the percentage of TB patients sampled, the proportion of clustered results plateaus at about 60 to 70% (1). It is
unlikely that more than a quarter of our study population would have had culture-positive, smear-negative TB, and therefore the impact of omitting these patients from our study should be relatively small.

REFERENCES


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